Summary of Safety and Effectiveness
Chilli® Cooled Ablation System
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Summary of Safety and Effectiveness Data

Chilli® Cooled Ablation System

Cardiac Pathways Corporation

1 GENERAL INFORMATION

Device Generic Name:	Cooled RF Ablation System
Device Trade Name:	Chilli® Cooled Ablation System
Device Model Numbers:	3005 Chilli® Cooled Ablation Catheter, Standard Curve 3006 Chilli® Cooled Ablation Catheter, Large Curve 8004 RF Generator and Pump System 2035 EGM Bypass Switch Box 2048 RF Filter Box 2100 Chilli® Tubing Kit
Name & Address of Sponsor:	Cardiac Pathways Corporation 995 Benecia Avenue Sunnyvale, CA 94086
PMA Application Number:	P980003
Date of Panel Recommendation:	July 21, 1998
Date of Notice of Approval to the Applicant:	February 2, 1999

2 INDICATIONS FOR USE

The Chilli Cooled Ablation System is indicated for:

- cardiac electrophysiological mapping;
- delivering diagnostic pacing stimuli; and
- radiofrequency ablation of mappable ventricular tachycardias attributable to ischemic heart disease or cardiomyopathy in patients who have failed drug therapy.

3 CONTRAINDICATIONS

Do not use this device in the following patients:

- patients with active systemic infection

- patients with a mechanical prosthetic heart valve through which the catheter must pass
- patients with left ventricular thrombus; or with left atrial thrombus or myxoma via the transseptal approach
- patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation

4 WARNINGS AND PRECAUTIONS

See WARNINGS AND PRECAUTIONS in the final draft labeling (Information for Use)

5 DEVICE DESCRIPTION

The Chilli® Cooled Ablation System (Chilli Cooled Ablation System) includes the Chilli Cooled Ablation Catheter (Chilli Catheter) and the Model 8004 Radiofrequency Generator/Pump System (Model 8004 RF Generator).

5.1 Chilli Cooled Ablation Catheter

The Chilli Catheter has a distal electrode segment and a proximal handle that are connected by a torquable catheter shaft. The electrode segment houses the tip electrode, the ring electrodes, and the temperature monitoring electrodes. The handle includes the electrical connector for the electrode wires, a knob used to deflect the tip, and two luer fittings used to connect the catheter to the fluid pump on the Model 8004 RF Generator and the fluid collection bag, respectively. The pullwire, electrode lead wires, and two lumens carrying cooling fluid pass through the shaft. The fluid pump on the Model 8004 RF Generator circulates cooling fluid through two lumens joined at the tip.

There are two different versions of the Chilli Catheter (see Table 5-1 below). Both catheters are built with the same materials and construction technique.

Table 5-1. Chilli Catheter Types

Model	Radius Range at 270° Deflection
Model 3005 Chilli Catheter (standard curve)	25 mm ± 2 mm
Model 3006 Chilli Catheter (large curve)	35 mm ± 2 mm

A separately packaged EGM cable is required for connecting the catheter to external stimulators, the Model 8004 RF Generator, and electrophysiologic recorders.

Pulling the deflection knob away from the catheter shaft causes the tip to deflect. Pushing the knob towards the catheter shaft straightens the tip. Rotating the entire handle to the left or right rotates the catheter tip in either direction. Fluid for cooling the catheter tip during ablation flows from the pump to the tip through one cooling lumen and back to the collection reservoir through the other cooling lumen.

5.2 Model 8004 RF Generator

The Model 8004 RF Generator is a constant frequency output (500 kHz sine wave), variable voltage power source that provides RF energy in the range of 0 - 50 Watts. RF energy is applied via unipolar delivery through the tip electrode of the Chilli Catheter and a return patch located on the patient's skin. The Chilli Catheter connection to the generator includes four electrode connections, a thermocouple sensor connection, and the cooling fluid connections.

The Model 8004 RF Generator operates in a constant power mode during the delivery of RF energy using a closed–loop feedback control which continuously monitors impedance, voltage, and current, then adjusts the voltage in order to maintain the target power setting.

The Pump that delivers the fluid to the Chilli Catheter tip has been integrated into the chassis of the Model 8004 RF Generator (i.e., mounted externally). An angiographic injector and syringe system circulates sterile fluid through catheter lumens.

Operator selections for ablation output parameters and limits monitored during ablation are summarized in Table 5-2.

Table 5-2. Adjustable Parameter Values

Adjustable Parameter	Value Range	Increment	Shipped/Default Value
Ablation Mode	Power		Power
Target Power	1 - 50 Watts	1 Watt	10 Watts
Target Duration	Off, 5 - 300 secs	5 seconds	30 seconds
Maximum Impedance Limit	100 - 500 Ohms	10 Ohms	200 Ohms
Minimum Impedance Limit	50 - 200 Ohms	10 Ohms	50 Ohms
Maximum Temperature in Power Mode	20 - 110 °C	1 °C	100° C
Maximum Duration if Target Duration is Off	0 - 295 seconds	1 second	120 seconds

5.3 Chilli Tubing Kit

The Chilli Tubing Kit connects the Chilli Catheter to the Pump System of the Model 8004 RF Generator and includes the collection system for used cooling fluid. Kit components include: the syringe that mounts on the Pump System; a dual check valve; the reservoir tube set; the delivery and disposal extension tube set; and the disposable bag set.

5.4 EGM Bypass Switch Box

The EGM Bypass Switch Box serves as a pass–through for the electrode signals from the Chilli Catheter and provides a mechanism for the clinician to switch the routing of the electrode signals between the Model 8004 RF Generator and the EGM recording instruments. The toggle switch setting determines the routing of catheter electrodes/signals.

5.5 RF Filter Box

The RF Filter Box allows EGM signals from the Chilli Catheter to be monitored during RF delivery. Cables connect the RF Filter Box to the Chilli Catheter, the Model 8004 RF Generator,

and the signal recording/display system. The switch setting determines whether the catheter electrodes/signals are filtered.

6 ALTERNATIVE PRACTICES AND PROCEDURES

Therapeutic options in patients with recurrent sustained VT include antiarrhythmic drug therapy, electrophysiologically guided ventricular surgery, and implantable cardioverter-defibrillators (ICD) on approved systems.

7 MARKETING HISTORY

The Chilli Cooled Ablation System has been marketed in Germany, the Netherlands, UK, France, Italy, Spain, Slovenia, Russia, Japan, and China.

There have been no countries from which the device has been withdrawn from marketing for any reason related to safety or effectiveness of the device.

8 ADVERSE EVENTS

Will be the same as the final product labeling.

9 SUMMARY OF PRECLINICAL STUDIES

Non-clinical bench testing and animal testing have been conducted to demonstrate the safety, reliability and performance specifications of the Chilli Cooled Ablation System. The following sections summarize the results of this testing.

9.1 Bench Testing – Model 8004 RF Generator

The electrical isolation of the Model 8004 RF Generator was tested in accordance with IEC 601-1 and AAMI HF18. The results are summarized in Table 9-1.

Table 9–1: Electrical Isolation Testing – Model 8004 RF Generator

Test	# of Units Tested	Acceptance Criteria	Results of Testing
Chassis leakage to ground	3	500 μA/100 μA	All samples passed
Patient leads (electrodes) to ground	3	50 μA/ 10 μA	All samples passed
Leakage current among patient leads	3	50 μA/ 10 μA	All samples passed
Leakage current due to external voltage	3	50 μA	All samples passed
Leakage current from accessory connections	3	500 μA/100 μA	All samples passed
High Voltage Tests	3	No arcing or current fluctuations	All samples passed
Leakage current at RF frequency of the device	3	150 mA = 30 V/200 Ohms	All samples passed

Power output at various loads that might be encountered in clinical use was assessed with the three systems under test. Testing was performed at 10, 30, and 50 Watts into loads of 50, 150, and 200 Ohms. The results are summarized in Table 9-2. In a steady state system, the closed loop power control operated as expected.

Table 9–2: Power Output Testing – Model 8004 RF Generator

Power (Watt)	Load	Voltage (Volt)		Impedance (Ohm)		Power (Watt)	
		A.C.	Results	A.C.	Results	A.C.	Results
10	50-Ohm	22.4 ± 2.2	All 3 Passed	50 ± 10	All 3 Passed	10 ± 1	All 3 Passed
	150-Ohm	38.7 ± 1.9	All 3 Passed	150 ± 20	All 3 Passed	10 ± 1	All 3 Passed
	200-Ohm	44.7 ± 4.5	All 3 Passed	200 ± 20	All 3 Passed	10 ± 1	All 3 Passed
30	50-Ohm	38.7 ± 3.9	All 3 Passed	50 ± 10	All 3 Passed	30 ± 1	All 3 Passed
	150-Ohm	67.0 ± 1.1	All 3 Passed	150 ± 20	All 3 Passed	30 ± 1	All 3 Passed
	200-Ohm	77.5 ± 7.5	All 3 Passed	200 ± 20	All 3 Passed	30 ± 1	All 3 Passed
50	50-Ohm	50.0 ± 5.0	All 3 Passed	50 ± 10	All 3 Passed	50 ± 1	All 3 Passed
	150-Ohm	86.6 ± 0.9	All 3 Passed	150 ± 20	All 3 Passed	50 ± 1	All 3 Passed
	200-Ohm	100 ± 10	All 3 Passed	200 ± 20	All 3 Passed	50 ± 1	All 3 Passed

A.C. = Acceptance Criteria

To verify the RF power output during closed-loop feedback control (power mode) of the instrument, a series of ablation outputs, each at a different setting, was performed with the three systems under test. The results are summarized in Table 9-3.

Table 9–3: Closed-loop Feedback Testing – Model 8004 RF Generator

Test	# of Units Tested	Acceptance Criteria	Results of Testing
Closed-loop feedback control test (power mode)	3	Ablation starts and stops when button is pressed or condition is met.	All samples passed
Temperature measurement	3	± 2°C	All samples passed

EGM signal pass–through and stimulation pass–through characteristics of the catheter electrode inputs through the Model 8004 RF Generator were assessed with the three systems under test over the frequency range 10 to 300 Hz, a typical frequency range for intracardiac signals. The results are summarized below.

Table 9–4: Pass-through Testing – Model 8004 RF Generator

Pass-Through Characteristic	# of Units Tested	Acceptance Criteria	Results of Testing
Amplitude	3	±3 dB	All samples passed
Peak noise	3	<250 μV	All samples passed
Cross Talk	3	< –40 dB	All samples passed

The integrity of analog output signals (power, temperature, impedance, voltage, and current) that may be monitored externally during ablation was evaluated with the three systems under test. The results are summarized in Table 9-5.

Table 9–5: Analog Output Testing – Model 8004 RF Generator

Analog Signal	# of Units Tested	Acceptance Criteria	Results of Testing
Power	3	Value: 0 - 1 V; Tolerance ±.01 V	All samples passed
Temperature	3	Value: 0 - 1 V; Tolerance ±.03 V	All samples passed
Impedance	3	Value: 0 - 1 V; Tolerance ±.01 V	All samples passed
Voltage	3	Value: 0 - 1 V; Tolerance ±.04 V	All samples passed
Current	3	Value: 0 - 1 V; Tolerance ±.02 V	All samples passed

To verify the proper performance of each limit detection function and the emergency switch, a series of ablation outputs were performed at different initial value settings for the Model 8004 RF Generator. In addition, an ablation stress test was performed to verify that power delivery was not impacted by high demand. Additionally, the expected operation of the injector pump after the integration of the pump electronics, pump power head, and pump interface software into the Model 8004 RF Generator was verified. The results are summarized in Table 9-6.

Table 9–6: System Testing – Model 8004 RF Generator

Test	# of Units Tested	Acceptance Criteria	Results of Testing
Limits Detection and Emergency Switch Test	3	Each stop mechanism must halt the delivery of RF output. The corresponding message identifying the stop mechanism must be displayed on the screen.	All samples passed
Ablation Stress Testing (step of 50 Watts for 295 seconds for 23 consecutive deliveries)	3	No failures or problems with power delivery	All samples passed
Pump Integration and Operation Test	3	Pump injects fluid to within 2 ml	All samples passed

Following sterilization, Chilli Catheters were subjected to the following tests:

Table 9–7: Electrical and Mechanical Testing – Chili Cooled Ablation Catheter

Catheter Tests Performed	# of Units Tested	Acceptance Criteria	Results
Final Inspection	35	Meet dimensional specs. Free from defects.	All samples passed
Electrical Continuity	35	No shorts or opens between electrodes and/or thermocouple	All samples passed
Resistance Measurements *	35	Electrode: <20 Ohm Thermocouple: <500 Ohm	All samples passed
Capacitance Measurements *	35	<1000 picoFarad	All samples passed
AC Impedance (5000 Hz) Measurements *	35	Attenuation of EGM signal < 0.1%	All samples passed
Dielectric Strength	34	Leakage current <0.30 mA	All samples passed

Catheter Tests Performed	# of Units Tested	Acceptance Criteria	Results
Flow	35	Sustain fluid flow rate of 36 ml/minute without exceeding 200 psi	All samples passed
Pressure (up to 300 psi)	35	No leaks	All samples passed
Cooling Efficiency	35	Tip temp. shall drop 20°C, in a 95°C water bath when 20-22°C cooling fluid is flowing through the catheter	All samples passed
Temperature Measurement	34	Reach 37 ± 1°C within 8 seconds. Reach 95 ± 3 C within 8 seconds.	All samples passed
Deflection (catheter placed in a simulated aortic arch, and the tip was deflected 180°)	30	No mechanical degradation or loss of electrical continuity after 50, 100, and 150 deflections	All samples passed
Insertion/Withdrawal Force (through a sheath)	34	< 3 lb; no bends or kinks in catheter	All samples passed
Handle–to–Shaft Interface (Strain Relief) Flex Bend	34	No mechanical or electrical damage after bending to a 1-inch radius of curvature 150 times.	All samples passed
Torsion Force and Turns to Failure	30	N/A	Average torsion force: 4.7 ± 0.9 in–oz; minimum 8 rotations before electrical failure
Proximal Shaft Flexural Rigidity Test	34	N/A	An average force of 2.76 ± 0.35 lb. was applied to the shaft in reducing the gage length by 0.250 in.

* Includes the electrode, the lead wire, the connector, and the EGM Cable

To verify that the joints and bonds of the catheter met the specifications, the following tensile testing was performed. For the testing of the Luer Fitting to the Handle bond, only one fitting from each device was tensile tested (The other fitting was used for testing torsion strength.).

Table 9–8: Tensile Testing – Chili Cooled Ablation Catheter

Joint/Bond	# of Units Tested	Minimum Tensile Strength	Results
Tip to Distal Tubing	34	1 lb	All samples passed
Tip to Pull–wire	34	3 lb	All samples passed
Distal Tubing to Distal Braided Tubing	34	3 lb	All samples passed
Distal Braided Tubing to Proximal Braided Tubing	34	3 lb	All samples passed
Distal Inner Extrusion to Proximal Inner Extrusion	34	3 lb	All samples passed
Proximal Tubing to Handle	33	3 lb	All samples passed
Pull–wire to Handle	34	3 lb	All samples passed
Distal Handle to Mid–Body Handle	34	3 lb	All samples passed
Mid–Body Handle to Proximal Handle	34	3 lb	All samples passed
Luer Fitting to Handle	34	3 lb	All samples passed
Handle to Lemo Connector	34	3 lb	All samples passed
Torsion strength of Luer Fitting to Handle	34	20 inch-oz	All samples passed

Biocompatibility Testing: Finished, EtO sterilized, Chilli Catheters were subjected to biocompatibility testing. Tests were selected in accordance with the requirements of ISO 10993-1.

Table 9–9: Biocompatibility Testing – Chili Cooled Ablation Catheter

Biocompatibility Study	# of Units Tested	Findings
Cytotoxicity, ISO Elution, L-929 Cells, 48 Hours	1	The MEM test extracts showed no evidence of causing cell lysis or toxicity. The negative controls, reagent controls, and the positive controls performed as anticipated. Under the conditions of this study, the MEM test extracts were not cytotoxic and passed this ISO study.
Sensitization Test in Guinea Pigs (Maximization Method); Saline extract and cottonseed oil extract	1	Under the conditions of this study, the SC and CSO test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig.
Acute Intracutaneous Reactivity Study in Rabbits; Saline extract and cottonseed oil extract	1	Under the conditions of this study, there was no evidence of significant irritation or toxicity from the extracts injected intracutaneously into rabbits. The Primary Irritation Index Characterization for the extracts was negligible (0.0 – SC, 0.1 – CSO).
Acute Systemic Toxicity Study in Mice; Saline extract and cottonseed oil extract	1	Under the conditions of this study, there was no mortality or evidence of significant systemic toxicity from the extracts. Each test article extract met the ISO requirements.
Material Mediated Pyrogen Study in Rabbits	1	Under the conditions of this study, the total rise of rabbit temperatures during the 3 hour observation periods were within acceptable USP limits. During the initial 3-rabbit study, one rabbit exhibited a 0.5°C temperature rise; a 5 rabbit retest of the test article was conducted. The extract was judged as nonpyrogenic based on the eight rabbit test results.

Biocompatibility Study	# of Units Tested	Findings
Hemolysis (ASTM) in Rabbit Blood	1	The negative and positive controls performed as anticipated. Under the conditions of this study, the mean hemolytic index for the test article extracts was 0%. The test article extracts were non-hemolytic.
Complement Activation in Normal Human Serum	1	Under the conditions of this assay, the test article indicated activation at 9,362 ng/ml. This was 6% of the normalized, positive control, and reference control materials performed as anticipated. The low biomaterial reference control (LDPE) indicated activation at 9,817 ng/ml or 8% of the normalized, positive control.
In Vivo Thromboresistance Study in the Dog (Venous Implant)	1	Under the conditions of the study, the test and control article resisted thrombogenicity.

To verify the durability of the cables, the following tests were performed on sterilized cables:

Table 9–10: Cables Testing

Cable Test	# of Units Tested	Acceptance Criteria	Results
Cable Flex Fatigue Test (Mil–C–27500G, General Specification for Power, Electrical and Shielded and Unshielded Cables)	14	Maintain electrical functionality. No cracking or splitting.	All samples passed
Cable Pull Tests: - Connector pin and each individual jacketed lead wire - Jacketed lead wires and the strain relief - 6–Pin Lemo connector and the cable	10	Strength >12 lb.	All samples passed
Dielectric Strength Tests (AAMI Standard ECGC–5/83, Standard for ECG Connectors)	20	Leakage current <0.25 mA	All samples passed

While the components of the Chilli Tubing Kit will not have any contact with the circulatory system under normal conditions, they would have some level of contact in the event of cooling fluid leakage from the catheter. These materials are ubiquitously used for manufacturing systems intended for infusing fluids into the circulatory system of humans.

The materials of the Chilli Tubing Kit have been subjected to assorted levels of biocompatibility testing by the Original Equipment Manufacturer (B. Braun). The following tests have been performed on some or all of the materials as appropriate: Cytotoxicity; Hemolysis; Material Mediated Pyrogenicity; Implant; USP Physicochemical; Irritation; Sensitization; Mutagenicity; Intracutaneous Toxicity; and Acute Systemic Toxicity Study. The materials passed all tests to which they were subjected.

The following electrical and functional testing was performed on the EGM Bypass Switch Box:

Table 9–11: EGM Bypass Switch Box Testing

EGM Bypass Switch Box Test	# of Units Tested	Acceptance Criteria	Results
Continuity/Resistance:	1		
Distal, Catheter to EGM Output		< 1 Ohm	Sample passed
Ring 2, Catheter to EGM Output		< 1 Ohm	Sample passed
Ring 3, Catheter to EGM Output		< 1 Ohm	Sample passed
Ring 4, Catheter to EGM Output		< 1 Ohm	Sample passed
TC +, Catheter to EGM Output		Open	Sample passed
TC –, Catheter to EGM Output		Open	Sample passed
Distal, Catheter to RF Generator		< 1 Ohm	Sample passed
Ring 2, Catheter to RF Generator		Open	Sample passed
Ring 3, Catheter to RF Generator		Open	Sample passed
Ring 4, Catheter to RF Generator		Open	Sample passed
TC +, Catheter to RF Generator		< 1 Ohm	Sample passed
TC –, Catheter to RF Generator		< 1 Ohm	Sample passed
Case to Lead Dielectric Withstand (IEC 601-1)	1	No arcing or popping	Sample passed
Lead to Lead Dielectric Withstand (AAMI ECG–5/83)	1	Leakage current <0.25 mA; No arcing or popping	Sample passed
AC (@5000 Hz) and DC Impedance	1	AC impedance >24 KΩ; DC impedance >100 MΩ	Sample passed
Affect on RF energy delivery and temperature measurement	1	Add < 5Ω to total impedance (10% attenuation); Maintain temperature accuracy (± 2°C)	Sample passed
Defibrillation Protection	1	Data received from the device before and after defibrillation energy is applied are the same.	Sample passed

The following electrical and functional testing was performed on the RF Filter Box:

Table 9–12: RF Filter Box Testing

Test	# of Units Tested	Acceptance Criteria	Results
Frequency Response (3 dB frequency, the –45° frequency, and the time delay)	1	3.742 kHz to 4.22 kHz; <0.5 msec time delay	Sample passed
RF Rejection	1	< 3 Volts Peak to Peak with 50W into 350 to 400 Ohm Load	Sample passed
Hi-Pot (IEC 601-1) in Monitor and Ablate Modes	1	No arcing or popping	Sample passed
Leakage Current (IEC 601-1) in Monitor and Ablate Modes	1	<10 μA/ <50 μA	Sample passed
Leakage Current due to external voltage in Monitor and Ablate Modes	1	<50 μA	Sample passed
Continuity in Monitor Mode and Ablate Mode	1	<1 Ω	Sample passed
Lead to Lead Dielectric Withstand	1	No arcing or popping	Sample passed
Filter Performance (Noise)	1	Distal to ring electrodes: 9.4 to 10.5 mVpp; Ring to ring electrodes < 20 μVpp	Sample passed
Common Mode Rejection	1	<3 mVpp	Sample passed
Over-Voltage Protection	1	2.6 V < Pos Saturation < 3.2 V; -2.6 V > Neg Saturation > –3.2 V	Sample passed
Common Mode Rejection with DC offsets and impedance imbalances	1	>100 dB	Sample passed
DC Impedance	1	56.7 MΩ to 110 MΩ	Sample passed
Bias evaluation	1	Between –10 mV DC and +10 mV DC	Sample passed
AC Impedance	1	> 450 kΩ @ 10 Hz, > 100 kΩ @ 100 Hz, and >25 kΩ @ 800 Hz	Sample passed
DC Leakage of filter inputs	1	–10 mV DC to +10 mV DC	Sample passed
Signal Quality in Monitor and Ablate Modes	1	Monitor Mode Noise <50 μVpp; Ablate Mode Noise <100 μVpp	Sample passed
Defibrillation Protection	1	Data received from the device before and after defibrillation energy is applied are the same.	Sample passed

9.2 Animal Testing

The Chilli Cooled Ablation System was evaluated in three separate acute studies: 1) Cooled versus Conventional Ablation; 2) Dose Response for Cooled Ablation; and 3) Catheter Signals and Pacing Thresholds.

9.2.1 Cooled versus Conventional Ablation

This study compared the incidence of impedance rises using cooled ablation to that using conventional ablation. It also defined the dose response curve for conventional and cooled ablation across the range of power levels commonly used in conventional ablation.

Six lesions were made in the left ventricle of each of eight mongrel dogs using the same power setting and delivery condition (cooled or conventional) selected for that animal.

The objectives of the study were as follows:

Table 9–13: Lesion Dimensions Statistical Data

			20 Watts	30 Watts	40 Watts	50 Watts
Width (cm)	Conventional Ablation	Mean	.78	.90	1.15	.87
		St. Dev.	.10	.09	.21	.12
	Cooled Ablation	Mean	.80	1.58	1.17	1.32
		St. Dev.	.09	.30	.27	.21
	two–tailed t–test		**NS**	**p < .001**	**NS**	**p = .001**
Depth (cm)	Conventional Ablation	Mean	.67	.67	.68	.60
		St. Dev.	.14	.33	.23	.26
	Cooled Ablation	Mean	.62	.62	.80	1.15
		St. Dev.	.08	.18	.11	.33
	two–tailed t–test		**NS**	**NS**	**NS**	**p = .009**
Volume (cm^3)	Conventional Ablation	Mean	.33	.34	.45	.35
		St. Dev.	.11	.13	.25	.25
	Cooled Ablation	Mean	.29	.84	.50	1.37
		St. Dev.	.08	.44	.06	.85
	two–tailed t–test		**NS**	**.024**	**NS**	**.018**

When using cooled ablation, the maximum duration of energy delivery began to become limited at 50 Watts.

Table 9-14: Energy Delivery Duration Statistical Data (seconds)

		20 Watts	30 Watts	40 Watts	50 Watts
Conventional	Mean	60	13	17	12
	St. Dev.	0	5.9	20.3	18.2
Cooled	Mean	60	60	60	28
	St. Dev.	0	0	0	17.4
two–tailed t–test		**NS**	**< .001**	**< .001**	**NS**

During the lesions analysis, no damage to adjacent vessels was observed.

The conclusions of this study were:

1. At 50 Watts cooled ablation created lesions that were wider, deeper, and of greater volume than conventional ablation.

2. Total energy delivery was higher using cooled ablation at 20, 30 and 40 Watts.
3. Impedance rises did not occur using cooled ablation until power delivery reached 50 Watts.

9.2.2 *Dose Response for Cooled Ablation*

The objectives of the study were:

1. To demonstrate that impedance rises using cooled ablation occur at a higher power level than would be expected with conventional ablation.
2. To prove the hypothesis that cooled ablation can make large lesions at the higher power levels.
3. To describe the dose response curve for RF energy.

Six to eight lesions were made in the left ventricles in each of twelve sheep. The lesions made in the left ventricle were made in approximately the same area in each animal to eliminate the effect of circulation differences within the ventricle.

The objective was to make a total of 72-96 lesions in twelve animals using four power levels: 40, 50, 60 and 70 Watts.

Table 9-15: Lesion Dimensions Across a Power Range (Watts); Statistical Data

		40 Watts (N=16)	50 Watts (N=17)	60 Watts (N=23)	70 Watts (N=21)
WIDTH (cm)	**Mean**	1.16	1.17	1.33	1.30
	St. Dev.	.30	.26	.34	.36
two-tailed t-test		**NS**	**NS**	**NS**	**NS**
DEPTH (cm)	**Mean**	.73	.78	.98	.71
	St. Dev.	.26	.30	.29	.27
two-tailed t-test		**.009**	**NS**	**.009**	**NS**
VOLUME (cm^3)	**Mean**	.61	.76	1.01	.71
	St. Dev.	.33	.30	.48	.44
two-tailed t-test		**.006**	**NS**	**.006**	**NS**

Conclusions of this study were as follows:

1. Lesion dimensions increased up to 60 Watts. Beyond 60 Watts, energy delivery was prematurely terminated by popping concomitant with an impedance rise. Total energy delivered flattened at 70 Watts, and no further lesion growth was realized because of popping concomitant with an impedance rise.
2. Cooled ablation reduced the incidence of coagulum mediated impedance rises, but popping occurred frequently at higher powers (60 Watts and above).

9.2.3 *Catheter Signals and Pacing Thresholds*

The objectives of the study were:

1. To test the safe operation of the cooled RF generator/catheter system across a range of power values up to maximum capability.
2. To make right and left ventricular lesions.
3. To collect and compare electrogram (EGM) signals from the tip and ring electrodes with signals from another commercially available mapping/ablation catheter.
4. To determine pacing thresholds and compare to a commercially available mapping/ablation catheter.

The following data assessments were made:

1. Signal quality assessment (signal amplitude and peak-to-peak noise) of EGM recordings from the Chilli Catheter and a commercially available mapping/ablation catheter (control catheter).
2. Comparison of pacing thresholds from the Chilli Catheter and a control catheter.

A total of seven catheters were used during this study. Signals were recorded in three sheep in both the right and left ventricle using the Chilli Catheter and a control catheter. Signal could not be recorded in the left ventricular artery (LVA) of one of the sheep because the catheter developed an open circuit to the tip electrode.

Recording (signal amplitude and noise) and pacing performance (pacing thresholds) were similar between the two models of the Chilli Catheter.

Conclusions of this study were as follows:

1. The signal quality of the Chilli Catheter was comparable to devices approved for commercial distribution.
2. The pacing performance of the Chilli Catheter was comparable to devices approved for commercial distribution.

9.2.4 *Chronic Animal Study*

The objectives of the study were as follows:

1. To test the safe operation of the Chilli Cooled Ablation System across a range of power values up to maximum capability.
2. To make right and left ventricular lesions.
3. To generate a dose response curve of power to lesion size.
4. To identify device problems/complications.
5. To collect and compare electrogram (EGM) signals from the tip and ring electrodes with signals from another commercially available mapping/ablation catheter.

6. To determine pacing threshold and compare to a commercially available mapping/ablation catheter.

Three sheep were studied, recovered from anesthesia, and allowed to survive for six to eight weeks.

Assessments are summarized in Table 9-16 and 9-17.

Table 9-16: Lesion Dimensions

Treatment Group		Volume (cm3)	Width (cm)	Depth (cm)
1 10 Watt	Mean	0.15	1.00	0.48
	Std Dev	0.10	0.08	0.20
30 Watt	Mean	0.24	1.07	0.50
	Std Dev	0.13	0.23	0.06
50 Watt	Mean	0.61	1.23	0.95
	Std Dev	0.26	0.22	0.21

Table 9–17: Pacing Threshold Comparisons

	Chilli Catheter	Control Catheter
Chronic Sheep 1	0.40 mA	0.65 mA
Chronic Sheep 2	0.45 mA	1.35 mA
Chronic Sheep 3	0.3 mA	0.5 mA
Mean	0.39 mA	0.84 mA
St. Dev.	0.08 mA	0.45 mA
P	.163	

Study conclusions included:

1. Lesion dimensions increased with power increase. The lesion sizes were in agreement with that reported in the literature. The standard deviation of lesion parameters was fairly large, which reflects the effect of catheter tip contact variability.
2. Catheter failures were noted and corrective action was taken. No generator failures occurred.
3. The endocardial signals recorded from the control catheter and the Chilli Catheter were comparable.
4. Right and left ventricular pacing thresholds from the control catheter and the Chilli Catheter were comparable.

10 CLINICAL INVESTIGATIONS

10.1 Objectives

A randomized prospective trial was conducted to compare acute and chronic reduction in spontaneous and inducible ventricular tachycardia (VT) following the ablation procedure to reduction during medical management.

Acute success was defined as an inability to induce mappable VT at the end of the ablation procedure. **Chronic success** was defined as freedom from spontaneous recurrence of any VT for six months following ablation.

10.2 Study Design

Cardiac Pathways sponsored a randomized, prospective clinical trial with a 3:1 randomization of ablation versus medical management, and two other treatment arms involving a total of 188 patients at 18 clinical sites.

The primary outcome measure was the absence of inducible mappable VT at the end of the ablation procedure. Secondarily, **long-term success** was the percent of patients in a study arm that were free of VT after and up to 6 months of follow-up.

The first nine patients were required to have an implantable cardioverter/defibrillator (ICD), either implanted prior to study entry or during the hospitalization at study entry, and to have failed antiarrhythmic drug therapy. For most of the study, patients were no longer required to have an ICD. For the first nine patients, the randomization ratio was 1:1; subsequently, the randomization ratio was 3:1 (ablation:control); and when randomization was discontinued. The requirement for failure of prior drug therapy evolved during the study. For most of the study, patients were required to have failed one antiarrhythmic drug.

10.3 Description of Patients and Gender Bias

A total of 188 patients were involved in clinical studies of the Chilli Cooled Ablation System (Table 10-1). All patients had ischemic heart disease or cardiomyopathy and had experienced a minimum of two episodes of spontaneous ventricular tachycardia (VT) in the two months prior to enrollment.

Table 10-1. Patient Cohorts of Clinical Studies

Patient Cohorts	Overall Patients Enrolled	Comparison of Randomized Patients	Patients Pooled for Safety
Randomized to ablation	75	75	65
Randomized to control	32	32	17
Emergency use	18	—	15
Nonrandomized ablation	63	—	53
Total enrollment	**188**	**107**	**150**

The 188 patients enrolled in the study ranged in age from 30 to 88 years with a mean 64 years; 92% were male. Inclusion criteria, exclusion criteria and study enrollment procedures were designed to avoid gender bias. This fraction of males enrolled was high, which is typical of ventricular tachycardia studies in patients with ischemic heart disease because of the prevalence of these conditions in males.

Table 10-2. Published major trials and the percent of males enrolled

Study	# Pts Enrolled	% Male	Citation
CASCADE—Cardiac Arrest in Seattle: Conventional Versus Amiodarone Drug Evaluation	224	89%	*Am. J. Cardiol.* 72:1295, 1993
ESVEM—Electrophysiology Study Vs. Electrocardiographic Monitoring	486	88%	*Circulation* 87:323, 1993
MUSTT—Multicenter UnSustained Tachycardia Trial	495 (inducible)	91%	*Circulation* 92:I-98, 1995

Success rates and adverse event rates were similar between males and females in this patient population, so the results presented are representative of both genders.

Demographic data for the pooled patients were similar to those of the randomized study. The patient population was predominantly male (92%), with ischemic heart disease (79%) and poor left ventricular function (mean ejection fraction 30.4%). They had very frequent VT episodes (mean $\pm$ SD. 24.8 $\pm$ 63.6), had previously failed an average of 2.5 drugs, 71% had ICDs, and 22% had undergone a previous unsuccessful catheter ablation attempt. Although changes to the inclusion criteria and study design occurred during the course of the study, this did not impact the homogeneity of the patient population. There were no differences in the patient characteristics among the cohorts. The comparability of the demographic data among cohorts supports the pooling of patients for analysis.

A mean of 3.0 different VTs were induced during the electrophysiology studies in pooled patients. VT was inducible in all but one patient. Ninety-seven percent of patients had inducible VT of cycle lengths greater than 300 msec. The inducibility of slower VT was higher in the pooled study compared to the randomized study, because the randomized study utilized intention-to-treat. Similar to the finding in the randomized study, 36% of pooled patients had VTs induced with cycle lengths of 300 msec or less (200 beats per minute or greater), suggesting that unmappable VTs were present in addition to the mappable ones.

10.4 Results

Of the 107 patients enrolled in the Randomized Trial, 75 were assigned to receive RF ablation and 32 to optimized antiarrhythmic drug therapy.

The Randomized Trial was analyzed by intention-to-treat; therefore, the analysis includes 10 patients who were randomized to ablation but did not receive ablation. Table 10-3 compares chronic success for patients randomized to RF ablation or antiarrhythmic drugs (control).

Table 10-3. Chronic (6 month) Success in the Randomized Trial

Percent [95% Confidence Interval], (Numerator/Denominator)
All patients enrolled in the Chilli Cooled Ablation System Study (N=107)

Chronic Success	Ablation Patients	Control Patients	Difference
No recurrence of any VT at 6 months	55% [43%, 66%] (41/75†)	19% [5.4%, 33%] (6/31‡)	35%* [17%, 53%]

95% confidence intervals by normal approximation

† Intention-to-treat includes 10 patients randomized to ablation who did not receive ablation treatment

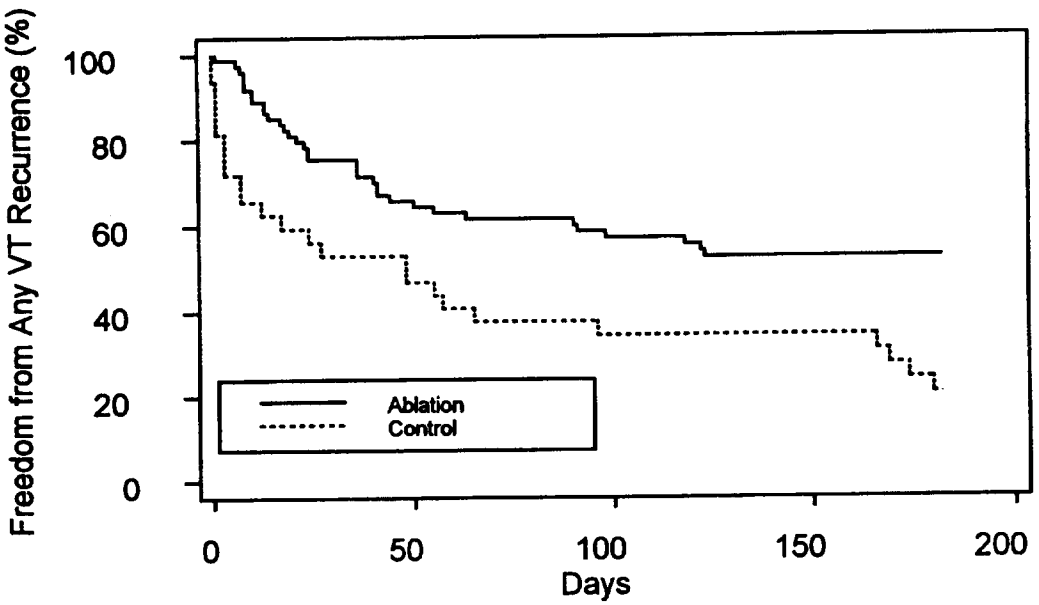
‡ One patient was lost to follow-up prior to six months and was excluded from analysis.

** Difference was statistically significant ($p<0.005$) by Fisher's Exact Test*

Control patients who crossed over to ablation (N = 17) were censored (removed from the survival analysis). Figure 10-1 shows the freedom from recurrence of any VT for both treatment groups in the Randomized Trial.

Figure 10-1: Freedom from VT Recurrence by Treatment*

All patients in the Randomized Trial, N=107



* Intention -to-treat includes 10 patients randomized to ablation who did not receive ablation treatment.

The difference in VT recurrence was statistically significant by the Gehan test (p = 0.0009).

Of the 150 patients in whom a Chilli Catheter was inserted, most (127) received ablation treatment on a single occasion, 18 were treated on two occasions, one patient on three occasions,

and four received no ablation treatment because the VT could not be mapped. Only the first treatment was considered in the effectiveness analyses. Table 10-4 lists the number of patients enrolled, treated, and the acute and chronic (six-month) success.

Table 10-4. Patient Cohorts and Ablation Success

All patients treated with the Chilli Cooled Ablation System (N=150)

Patient Cohort	No. of Patients Ablated	Acute Success		Chronic Success	
		Number	Percent	Number	Percent
Randomized to ablation	65	46/65	71% [60%, 82%] *	36/65	55% [43%, 68%]
Control cross-over	17	14/17	82% [57%, 96%]	12/17	71% [44%, 90%]
Emergency use	15	7/10†	70% [35%, 93%]	8/15	53% [27%, 79%]
Nonrandomized	53	42/53	79% [68%, 90%]	22/43‡	51% [36%, 66%]
Total	150	109/145	75% [68%, 82%]	78/140	56% [48%, 64%]

* [95% confidence intervals by exact method]

† Acute success not assessed in five patients

‡ Six-month follow-up not available in 10 patients

Acute clinical success was 75% for the pooled patients and was similar among cohorts. The long-term success rate was 56% for the pooled patients and was similar among cohorts. The acute and long-term success rates were similar to the findings in the randomized study. Univariate analysis was performed on clinical variables, but no clinical characteristic was predictive of acute success.

Reduction in VT Episodes

The frequency of VT episodes in the two months before and after ablation was compared in the pooled patients. In the two months before ablation, the (mean ± SD) number of VT episodes in pooled patients was 26 ± 66, compared to 7.1± 34. The decrease in VT episodes with ablation was highly significant($p = 0.001$). In 73% of the patients, the density of VT episodes was reduced by at least 75%.

The reduction in VT episodes was statistically significant in patients in whom the ablation was an acute success, but not in patients in whom it was an acute failure.

The induction of VT with programmed stimulation was assessed at 2-3 months follow-up (N=61). VT was inducible in 67%, but clinical VT was inducible in only 10% of the patients.

The 150 patients treated with ablation underwent a total of 166 procedures, including repeat procedures for VT recurrence. Patients had CK-MB enzyme levels drawn at baseline, and at 1-4 and 12-24 hours after ablation. Mean CK-MB levels increased by 9.7 at 1-4 hours and 17 at 12-24 hours.

The mean total procedure time was 284 minutes, with a mean total fluoroscopy time of 54 minutes. A mean of 12 ± 10 lesions were delivered per procedure (median 9 lesions and range of 1-69 lesions). The mean maximum power delivered was 36 Watts for a mean of 63 seconds' duration. The mean maximum impedance was 135 Ohms. Only 0.9% of energy deliveries were reported to occur with an audible pop. The mean maximum temperature attained was 44°C. The temperature range from 40-45°C was most often correlated with other evidence of adequate lesion development.

11 CONCLUSIONS DRAWN FROM STUDIES

The preclinical testing demonstrates that the catheter should maintain its mechanical and electrical integrity and that the patient-contacting materials should be biocompatible, under the proposed conditions of use. The clinical data provide reasonable assurance that the Cardiac Pathways Corporation's PMA for the Chilli Cooled Ablation System is reasonably safe and effective for the treatment of SVT under the proposed conditions of use.

12 PANEL RECOMMENDATION

At an advisory meeting held on July 21, 1998, the Circulatory System Devices Panel recommended that Cardiac Pathways Corporation's PMA for the Chilli Cooled Ablation System be approved subject to submission to, and approval by, the Center for Devices and Radiological Health (CDRH) the following:

1. Changes in the labeling (INDICATIONS, PATIENT COUNSELLING, and INDIVIDUALIZATION OF TREATMENT); and
2. Agreement to conduct a postapproval study must be conducted to obtain a usage registry of patients receiving treatment with the Chilli® Cooled Ablation System to analyze the following risk factors on safety and effectiveness:
    a) Estimated ejection fraction;
    b) Age;
    c) Prior failed ablation of VT;
    d) Concomitant antiarrhythmic drug treatment; and
    e) ICD implant prior to or following ablation.

13 FDA DECISION

FDA concurred with the Circulatory System Devices Panel's recommendation of July 21, 1998, and issued a letter to Cardiac Pathways Corporation, advising that its PMA was approvable subject to the labeling changes recommended by the Panel and required by FDA.

FDA performed an inspection and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

14 APPROVAL SPECIFICATIONS

Directions for Use: See Final Draft Labeling (Information for Use)

Hazards to Health from Use of the Device: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the Final Draft Labeling (Information for Use).

Post-approval Requirements and Restrictions: See Approval Order